Suicidality and antidepressants in the elderly

David W. Crumpacker, MD

Suicide has reached epidemic proportions in the elderly, particularly in non-Hispanic white men. Unfortunately, the risk is underappreciated in this population. Known risk correlates for suicide in this population fall into three interrelated categories. Sociologic factors include such considerations as living alone and having few social interactions. Physical health factors include having more medical comorbidity and being a current smoker. The mental health risk factors include the presence of mood and anxiety disorders with a focus on the greater severity of symptoms, especially hypersomnia, hopelessness, and a history of suicide attempts. Suicide is a spectrum comprising ideation, intent, and plan. Clinical depression is never a normal part of aging and warrants aggressive treatment. Recent warnings linking antidepressants and suicide may have special relevance in the elderly. Based on preliminary studies with antipsychotic drugs, a subgroup of patients who experience akathisia may be particularly vulnerable to suicide. Upon initiation of antidepressants, it is recommended that adults be seen in follow-up three times within the first 12 weeks of treatment; if medically indicated, the first contact should be during the first week.

Suicide is a complex issue that is incompletely understood. Various epochs and cultures have viewed it differently. It has included the political statement and the culturally accepted and expected response to public shame. History has given us many dramatic examples: the rape and suicide of Lucretia in ancient Rome, the seppuku of the samurai, the suicides of Nazi leaders in World War II, and the self-immolation of Thich Quang Duc to protest the persecution of Buddhists in the 1960s. Indeed, Manet's *Suicide* may depict Werther of Goethe's *Die Leiden des Jungen Werther* (1), a story that came to life in numerous operas and ballets and that led to the term *Werther-Fieber,* "Werther fever," understood as copycat suicides. Such copycat suicides have particularly been evident on the Golden Gate Bridge, the site of 1300 suicides—nearly one every 2 weeks—since it opened in 1937 (2). In addition, various aspects of mental health impact suicide rates worldwide. This article focuses on the role played by mental illness in suicide—with a focus on the elderly, defined as those ≥65 years of age.

The elderly face numerous challenges and changes: loss of work and self-esteem, inactivity, medical illness, and loss of loved ones, to mention but a few. Notwithstanding, depression is never a normal part of aging. Frequently, polypharmacy confounds diagnosis and treatment of mental illness in the elderly. Unfortunately, the risk of suicide is underappreciated in this population. Thus, it should be evaluated along a continuum—from ideation, intent, and plan to attempts and completion. This article explores known risk correlates of suicide in this population: epidemiologic and demographic factors as well as social, physical, and mental health aspects. The article then reviews the relationship between suicidal manifestations and antidepressants and concludes with a practical management strategy for the elderly given the current evidence base.

EPIDEMIOLOGY OF SUICIDE

In the general population, suicide is the 11th leading cause of death, with a rate of 10.4 per 100,000 (3). While seniors comprise 12% of the US population, they accounted for 16% of suicide deaths in 2004. The rate per 100,000 increases with age: it is 14.3 in those ≥65 years, 17.6 in those 75 to 84 years, and 49.8 in non-Hispanic white men ≥85 years—nearly five times the rate of the general population. Thus, in these groups of seniors, suicide has reached epidemic proportions.

Suicide rates vary by US region, with suicide more prevalent in the West and least prevalent in the Northeast *(Figure 1).* Worldwide, suicide rates are highest in the former Soviet Union, most of Europe and Scandinavia, China, and Australia and are lowest in Mexico, Central America, and South America.

The elderly are most likely to be successful in a suicide attempt. While young adults have one completed suicide per 200 attempts, the elderly have one suicide per four attempts (3). Therefore, the elderly patient with suicidal ideation, intent, or plan should be taken very seriously.

SOCIAL HEALTH RISK FACTORS FOR SUICIDE

In their study of risk factors for suicide in later life, Conwell and colleagues highlighted two social risk factors: living alone

From the Department of Psychiatry, Baylor University Medical Center, Dallas, Texas.

Presented at internal medicine grand rounds at Baylor University Medical Center, May 13, 2008.

Corresponding author: David W. Crumpacker, MD, 3600 Gaston Avenue, Suite 1155, Dallas, Texas 75246 (e-mail: drcrumpacker@swbell.net).

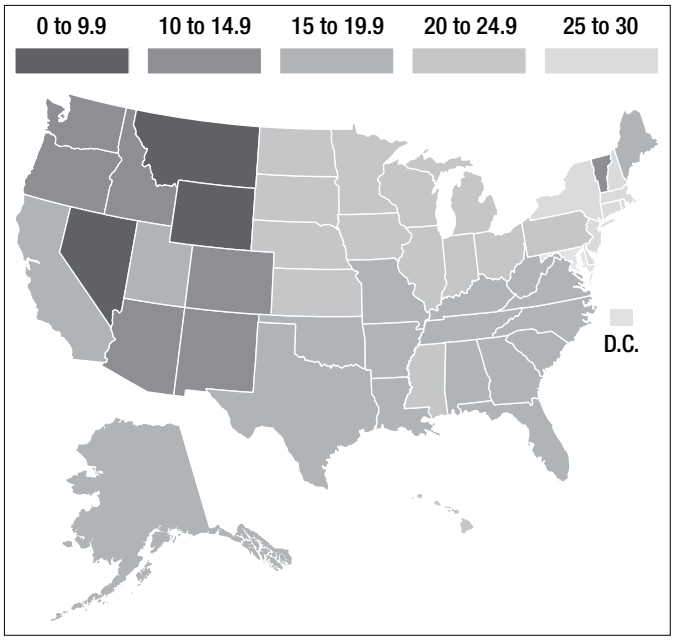

Figure 1. Suicides per 100,000 persons aged 65 and older, 1999–2004. Source: Centers for Disease Control and Prevention.

and low social interactions (4). They further noted that the effect of stressful life events was mixed, especially when mood disorders were factored out.

The issue of social connectedness has been considered for decades. Sociologist Émile Durkheim studied suicide in the late 1800s and proposed that a person's connectedness within the social environment might determine his or her potential of committing suicide. This social integration varies from society to society and with individuals within these social networks (5, 6). Among other findings, Durkheim reported in his seminal work, *Suicide* (1897), that suicide rates were higher in widowed, single, or divorced persons (5). Additionally, suicide rates have been found to be highest in white men, followed by black men, then white women, and finally black women. This trend, in fact, may reflect varying degrees of social integration among these subsets of the population *(Figure 2)*. These social factors, therefore, must be explored among elderly patients.

PHYSICAL HEALTH RISK FACTORS FOR SUICIDE

Aspects of physical health—including being a current smoker and having more medical comorbidity—are also implicated as risk factors for suicide in seniors (4). Interestingly, degree of impairment has had a mixed correlation with suicide. It may be that the most impaired, such as those who are paralyzed, are not physically able to commit suicide. On the one hand is the case of Nancy Crick. After a successful resection of her colon cancer, she ended her life in 2002 assisted by the euthanasia device developed by Australian physician Philip Nitschke (born 1947). Autopsy revealed sigmoid volvulus and surgical adhesions that the coroner ruled were treatable and not terminal conditions.

Table. Mental health risk factors for suicide in the elderly

• Presence of a mood disorder, such as depression
• History of attempts
• Suicide ideation
• Greater severity of symptoms
• Hypersomnia (≥9 hours per night)
• Hopelessness
• Comorbid anxiety and panic
• Personality disorders (more neurotic and less open)
• Possibly, substance use disorders*

*The findings on the role of substance use disorders were inconsistent among the elderly, but substance abuse was clearly a factor in younger adults.

MENTAL HEALTH RISK FACTORS FOR SUICIDE

While social and physical health affect suicide, mental health plays a key role. Research has identified the most common mental health factors associated with suicide in the elderly *(Table)* (4, 6). These factors include the presence of a mood disorder such as depression; a history of attempts, particularly since the completion rate among seniors is so high; anxiety disorders; greater severity of symptoms; hypersomnia; and hopelessness. Personality disorders are a factor in seniors but less so than in other groups since such disorders are not conducive to a long life.

The impact of substance use on suicide has mixed data in seniors, although it is a clear risk factor in other age groups. The use of alcohol is a silent illness in this group, and many seniors use alcohol to control pain and depression. At the same time, seniors often cannot tolerate alcohol as well as younger people do.

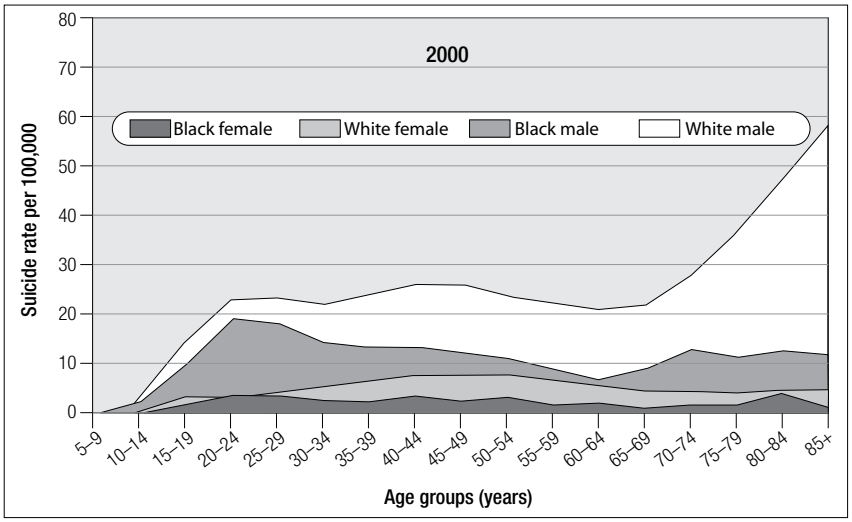

Figure 2. Suicide rates by age and sex, with data confirming Durkheim's hypothesis that groups with less social connectedness would have higher suicide rates. Source: National Institute of Mental Health. Data from the Centers for Disease Control and Prevention, National Center for Health Statistics.

Depression

It is never *normal* to be depressed. Clinical depression is never a natural sequela of any medical illness. Indeed, it is not associated with the aging process at all. Prevalence of depression, in fact, drops with increasing age. Estimates of major depression among seniors in the community range from 1% to 5%—a rate lower than that in younger adults. However, the rate skyrockets to 11.5% among hospitalized elderly and 13.5% among elderly who require home health (7–9). Evidently, most seniors in the community never have a depressive episode.

Depression increases the morbidity and mortality of every medical illness. Obviously, should depression arise in the senior, treatment should be as immediate and aggressive as for the younger patient. Up to 75% of older adults who complete suicide visited a physician within a month before death. The risk of depression increases when other illnesses are present and when function becomes impaired. In addition, subsyndromal or minor depression is also a risk factor for developing major depression, particularly in seniors. Perhaps 5 million elderly people suffer from subsyndromal depression.

USE OF ANTIDEPRESSANTS AND THE RISK OF SUICIDE

The desire to treat depression in seniors raises new questions, particularly since some studies have suggested a link between antidepressant treatment and increased risk of suicide in children and adolescents. These studies have led to warnings in treating this subset of the population. If seniors are already at increased risk of untreated depression and completed suicide, then these findings should be considered in this population as well.

In general, the role of antidepressants is to ameliorate the symptoms of depression and anxiety—both of which are risk factors for suicide (10). Since its approval by the Food and Drug Administration (FDA) in December 1987, fluoxetine hydrochloride (Prozac) demonstrated an unknown median lethal dose. In other words, patients couldn't overdose on this medicine as they could with tricyclic antidepressants (TCAs). Similar results have been shown for other selective serotonin reuptake inhibitors (SSRIs), e.g., citalopram and sertraline, and the serotonin-norepinephrine reuptake inhibitors, e.g., venlafaxine and duloxetine. The unintended consequence is the conception that since these drugs are safer than TCAs and monoamine oxidase inhibitors, therefore they must be benign as well. Regrettably, this has led to a dearth in research on somatic treatments of depression, such as electroconvulsive therapy, vagal nerve stimulation, transcranial magnetic stimulation, and light therapy. Therefore, the initial studies linking serotonin reuptake inhibitors with suicide arose within this construct. Thus, the original purpose was to demonstrate that these agents are not benign.

The beginning of this thread of reasoning was Donovan's study in the United Kingdom, which was published in 1999 (11). Using data on 222 suicides from 1990 to 1994 from three regions of Britain and Ireland, he determined that 41 (18.5%) of the cases had been prescribed one antidepressant within a month of suicide. Suicide by any method was more likely to occur following the prescription of SSRIs than of TCAs. Needless to say, a temporal link does not imply causality; perhaps the explanation was that SSRIs were preferentially prescribed to patients at a higher *risk* of suicide.

Follow-up studies in the UK confirmed many of Donovan's findings. However, studies in the USA have been mixed. For example, Olfson and colleagues found an inverse relationship between regional use of antidepressants and suicide in youth—that is, increased antidepressant use was associated with decreased suicide rates. They concluded that there is a role for antidepressant treatment in youth suicide prevention efforts, especially for males, older adolescents, and adolescents who reside in lower-income regions (12).

Based on the initial collection of data, official organizations in the USA and UK issued warnings about antidepressant use in children and adolescents. Subsequently, the number of antidepressant prescriptions dropped by 20% in the USA and 40% in the UK between 2003 and 2004 (13).

More recent studies, however, raise doubts about an association between suicide rates and changes in antidepressant prescribing. The most recent US data suggest that adolescent suicide deaths began to decrease when antidepressant use increased between 2004 and 2005 (14). Further studies in the UK have not replicated Donovan's findings, but rather show a lack of connection between antidepressant prescribing rates and suicide rates in adolescents and young adults in the UK. Suicide rates declined when antidepressant use steadily increased but continued to decline at the same rate when the use of antidepressants fell sharply in 2003 and 2004.

In addition, other studies (15–18) have shown that the risk of suicidal behavior after starting antidepressant treatment may be similar among users of amitriptyline, fluoxetine, and paroxetine, and there may be no substantial difference in the effect of the newer drugs (SSRIs) on people aged 10 to 19 years. Furthermore, these studies suggest that the risk of suicidal behavior may be increased only in the first month after starting medication, especially during the first 9 days. Additionally, it was rare for patients to develop suicidal behavior *de novo* after that initial period (15–18).

Data in the elderly

In general, it is believed that SSRIs may increase impulsive acts; the elderly, indeed, might be as vulnerable as youth to these effects. In fact, the elderly may be even more sensitive to the effects of drugs, given pharmacodynamic and pharmacokinetic changes associated with aging. These include a decreased blood-brain barrier, decreased phase I and phase II metabolism, and decreased renal clearance of drugs as aging occurs. A limited number of studies have specifically addressed the risk of suicide following antidepressant use in the elderly.

In 2006, Barak and colleagues published a retrospective case-control study. Of their 202 patients with major depressive disorder treated over a 10-year period, antidepressants had been prescribed more often in the control group than in the group that went on to commit suicide (29% vs 21%; $P = 0.03$). They concluded that elderly depressed patients treated with antidepressants might be at reduced risk of attempting suicide (19).

Other studies have supported this conclusion (20–22). While SSRIs may be associated with increased impulsive acts, treatment with SSRIs has been shown to decrease the overall risk of suicide, particularly in elderly men. Increased rates of antidepressant prescription may decrease the risk of suicide, even in hospitalized patients. Indeed, the benefits could well outweigh the risks.

Several meta-analysis SSRI trials have shown an increased risk of self-harm; effectively, they have not ruled out an increased risk of suicide caused by SSRIs (23, 24). When prescribing SSRIs, clinicians should warn patients of the possible risk of suicidal behavior and monitor patients closely, especially in the early stages of treatment. It may be that initiation of SSRI therapy is associated with an increased risk of suicide during the first month of therapy compared with other antidepressants. While the absolute risk is low, this suggests that an idiosyncratic response to these agents may provoke suicide in a vulnerable subgroup of patients.

Identifying subsets of patients vulnerable to adverse events

It is likely that effects of antidepressants on suicidal ideation or suicide risk differ across individuals. Most experienced clinicians have heard patients describe sudden onset of agitation and suicidal thoughts after starting antidepressants. The initial advisory from the FDA was motivated in part by numerous similar reports (25–28). While these anecdotes cannot prove causation, they certainly suggest that some patients may be especially sensitive to this particular adverse effect. Even if randomized trials and large observational studies find no effect of antidepressants on average rates of suicide attempt or suicide death, average effects may not apply to all individuals.

A clue to finding this subset may be found in recent studies in the antipsychotic literature. These studies have explored the well-established link between antipsychotic drugs and akathisia (27). Akathisia is a subjective sense in the muscles, frequently the large muscles of the legs, of the need to move around. In case reports (29, 30), researchers found a link between akathisia and suicidal ideation after patients took antipsychotic drugs. Atbasoglu and colleagues examined this link in 68 patients (31). Significantly more patients who were suicidal reported the symptom of akathisia. Similarly, significantly more patients who had akathisia reported being suicidal *(Figure 3).*

It is well established in the literature that antidepressants are associated with akathisia (32). It may be that a subgroup of patients prone to akathisia with antidepressant treatment is at increased risk of suicidal behavior. Young adults and the elderly demonstrate a greater vulnerability to akathisia than other groups. Understandably, patients may lack the vocabulary to describe this adverse event. They might report agitation or simply act out.

Further research is needed to draw more definite conclusions.

CLINICAL IMPLICATIONS

Elderly patients show a preference for going to their primary care physicians. This translates frequently into more medication, less psychotherapy, and less social support for the symptoms of depression (3). Physicians who see these patients need to consider the warning from the FDA: adult patients should be monitored closely for worsening depression and increased suicidality and behavior (25, 26).

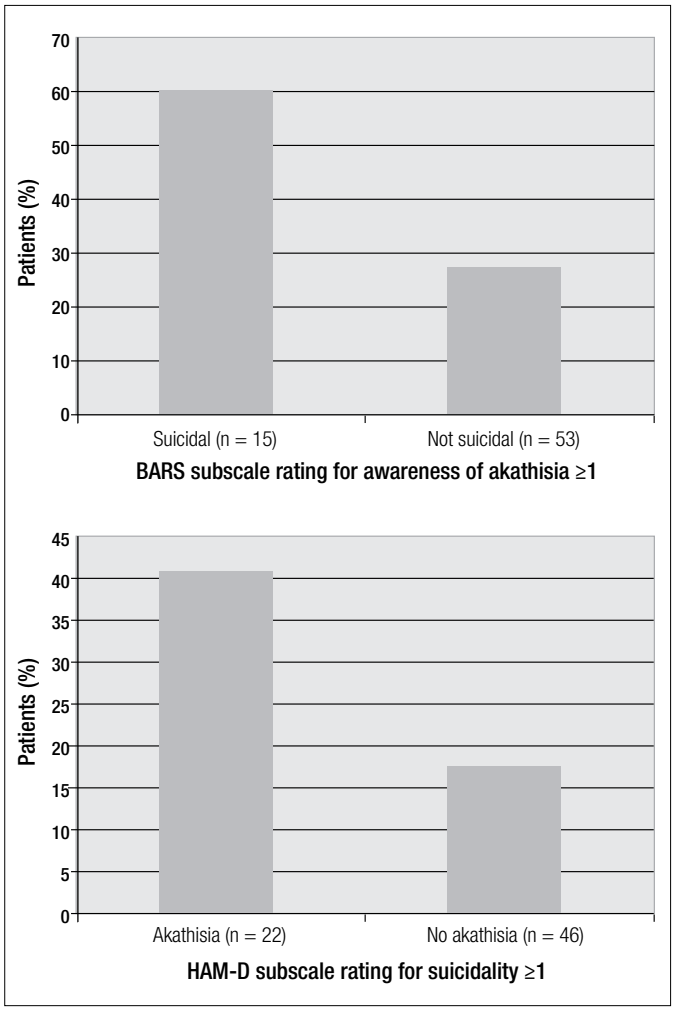

Figure 3. Association between suicidality and akathisia. Data from Atbasoglu EC et al (31). HAM-D indicates Hamilton Depression Scale; BARS, Barnes Akathisia Rating Scale.

What should such monitoring consist of? The National Committee for Quality Assurance suggested three contacts during the first 12 weeks of acute treatment, with the initial follow-up contact within the first week (33). Data show that it is unusual for patients to develop suicidal ideation months after therapy; if it is going to happen, it usually occurs within that first month.

For patients who experience suicidal ideation after taking antidepressants, it is incumbent upon the clinician to explore to what extent the patient has ideation, intent, and plan. Suicidal ideation without intent and plan may require only supportive intervention, such as involvement of family and social networks. Were the patient to show a high degree of intent, it would be appropriate to call a psychiatrist. Automatic discontinuation of the antidepressant may not be the best approach. The patient who experiences akathisia within this context may require discontinuation of the compound and psychiatric intervention. In addition, patients with a history of suicide attempts deserve higher scrutiny.

SUMMARY

Suicide is a complex issue—a spectrum ranging from ideation to intent and plan. Furthermore, not all patients with ideation attempt suicide. In addition, suicide is reaching epidemic proportions in non-Hispanic white men, particularly as they age. Depression is a treatable challenge; it should not be considered a normal part of aging. Antidepressants have been demonstrated to ameliorate the symptoms of depression. Unfortunately, a subset of the population, albeit small, may be at increased risk of suicide when treated with some antidepressants. Nonetheless, there is an extensively demonstrated literature into the overall benefits to the general population who receive antidepressant treatment. In recognizing this, it is incumbent upon the clinician to identify this subset and not penalize the entire population by denying effective care. Akathisia may play a role in distinguishing those at risk. Further research is necessary.

1. Goethe JW. *Die Leiden des jungen Werther*. Anaconda, 2005.
2. King J. Lethal beauty: suicides by location. *San Francisco Chronicle,* November 4, 2005.
3. National Center for Injury Prevention and Control. Web-based Injury Statistics Query and Reporting System (WISQARS) [online]. Atlanta, GA: Centers for Disease Control and Prevention, 2005. Available from www.cdc.gov/ncipc/wisqars; accessed April 10, 2008.
4. Conwell Y, Duberstein PR, Caine ED. Risk factors for suicide in later life. *Biol Psychiatry* 2002;52(3):193–204.
5. Durkheim É. *On Suicide*. Stennet R, Riley A, Buss R, eds. New York: Penguin Classics, 2007.
6. Conwell Y, Brent D. Suicide and aging. I: Patterns of psychiatric diagnosis. *Int Psychogeriatr* 1995;7(2):149–164.
7. Conwell Y. Suicide in later life: a review and recommendations for prevention. *Suicide Life Threat Behav* 2001;31(Suppl):32–47.
8. Hybels CF, Blazer DG. Epidemiology of late-life mental disorders. *Clin Geriatr Med* 2003;19(4):663–696.
9. Narrow WE. One-year prevalence of mental disorders, excluding substance use disorders, in the U.S.: NIMH ECA prospective data. Population estimates based on U.S. Census estimated residential population age 18 and over on July 1, 1998. Unpublished.
10. Alexopoulos GS. Mood disorders. In Sadock BJ, Sadock VA, eds. *Comprehensive Textbook of Psychiatry*, 7th ed., vol. 2. Baltimore: Williams & Wilkins, 2000.
11. Donovan S, Kelleher MJ, Lambourn J, Foster T. The occurrence of suicide following the prescription of antidepressant drugs. *Arch Suicide Res* 1999;5(3):181–192.
12. Olfson M, Shaffer D, Marcus SC, Greenberg T. Relationship between antidepressant medication treatment and suicide in adolescents. *Arch Gen Psychiatry* 2003;60(10):978–982.
13. Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Erkens JA, Herings RM, Mann JJ. Early evidence on the effects of regulators' suicidality warnings on SSRI prescriptions and suicide in children and adolescents. *Am J Psychiatry* 2007;164(9):1356–1363.
14. Biddle L, Brock A, Brookes ST, Gunnell D. Suicide rates in young men in England and Wales in the 21st century: time trend study. *BMJ* 2008;336(7643):539–542.
15. Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *JAMA* 2004;292(3):338–343.
16. Martinez C, Rietbrock S, Wise L, Ashby D, Chick J, Moseley J, Evans S, Gunnell D. Antidepressant treatment and the risk of fatal and non-fatal self harm in first episode depression: nested case-control study. *BMJ* 2005;330(7488):389.
17. Simon GE, Savarino J, Operskalski B, Wang PS. Suicide risk during antidepressant treatment. *Am J Psychiatry* 2006;163(1):41–47.
18. Wessely S, Kerwin R. Suicide risk and the SSRIs. *JAMA* 2004;292(3):379–381.
19. Barak Y, Olmer A, Aizenberg D. Antidepressants reduce the risk of suicide among elderly depressed patients. *Neuropsychopharmacology* 2006;31(1):178–181.
20. Healy D, Whitaker C. Antidepressants and suicide: risk-benefit conundrums. *J Psychiatry Neurosci* 2003;28(5):331–337.
21. Barak Y, Aizenberg D. Association between antidepressant prescribing and suicide in Israel. *Int Clin Psychopharmacol* 2006;21(5):281–284.
22. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004;363(9418):1341–1345.
23. March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J; TADS Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA* 2004;292(7):807–820.
24. Juurlink DN, Mamdani MM, Kopp A, Redelmeier DA. The risk of suicide with selective serotonin reuptake inhibitors in the elderly. *Am J Psychiatry* 2006;163(5):813–821.
25. Food and Drug Administration. Psychopharmacologic Drugs Advisory Committee and Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee: Slides. February 2004. Available at www.fda.gov/ohrms/dockets/ac/04/slides/4006s1.htm; accessed April 10, 2008.
26. Moynihan R. FDA advisory panel calls for suicide warnings over new antidepressants. *BMJ* 2004;328(7435):303.
27. Nasrallah HA, Brecher M, Paulsson B. Placebo-level incidence of extrapyramidal symptoms (EPS) with quetiapine in controlled studies of patients with bipolar mania. *Bipolar Disord* 2006 ;8(5 Pt 1):467–474.
28. Simon GE. How can we know whether antidepressants increase suicide risk? *Am J Psychiatry* 2006;163(11):1861–1863.
29. Hung YC, Ho YY, Shen CL. Delayed akathisia and suicidal attempts following epidural droperidol infusion—a case report. *Acta Anaesthesiol Sin* 1999;37(3):151–154.
30. Drake RE, Ehrlich J. Suicide attempts associated with akathisia. *Am J Psychiatry* 1985;142(4):499–501.
31. Atbasoglu EC, Schultz SK, Andreasen NC. The relationship of akathisia with suicidality and depersonalization among patients with schizophrenia. *J Neuropsychiatry Clin Neurosci* 2001;13(3):336–341.
32. Hansen L. Fluoxetine dose-increment related akathisia in depression: implications for clinical care, recognition and management of selective serotonin reuptake inhibitor-induced akathisia. *J Psychopharmacol* 2003; 17(4):451–452.
33. National Committee for Quality Assurance. HEDIS Volume 2: Technical Specifications. Washington, DC: 2004.